UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,095	04/13/2005	Manfred Windisch	4301-1117	4495

466 7590 04/05/2007

YOUNG & THOMPSON
745 SOUTH 23RD STREET
2ND FLOOR
ARLINGTON, VA 22202

EXAMINER	
WANG, CHANG YU	
ART UNIT	PAPER NUMBER
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,095	WINDISCH, MANFRED	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24 and 27-29* is/are pending in the application.

4a) Of the above claim(s) *10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11-24 and 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

Status of Application/Amendments/claims

1. Applicant's amendment filed January 16, 2007 is acknowledged. Claims 25-26 are cancelled. Claims 1-24 and newly added claims 27-29 are pending in this application. Claim 10 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

2. Claims 1-9, 11-24 and 27-29 are under examination in this office action.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed on January 16, 2007 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Specification

5. The objection to the specification because of sequence identifiers is withdrawn in response to Applicant's argument.

Claim Rejections/Objections Withdrawn

6. The rejection of claims 1-9 and 11-24 under 35 U.S.C. 112, first paragraph, for failing to meet the written description is withdrawn in response to Applicant's amendment to the claims.

The rejection of claim 14 under 35 U.S.C. 112, second paragraph, for being indefinite because of the recitation "all states" is withdrawn in response to Applicant's amendment to the claims.

The rejection of claims 1, 2, 5 and 7-24 under 35 U.S.C. 102(b) for being anticipated by WO200160794 (published Aug 23, 2001, PCT/US01/05569, filed Feb 20, 2001, priority date Feb 18, 2000) is withdrawn in response to Applicant's amendment to the claims.

The rejection of claims 1-3 under 35 U.S.C. 103(a) for being unpatentable over WO200160794 (published Aug 23, 2001, PCT/US01/05569, filed Feb 20, 2001, priority date Feb 18, 2000) in view of Volkmann et al. (EXS, 1998, 85: 87-105) is withdrawn in response to Applicant's amendment to the claims.

The rejection of claims 1 and 4-6 under 35 U.S.C. 103(a) for being unpatentable over WO200160794 (published Aug 23, 2001, PCT/US01/05569, filed Feb 20, 2001, priority date Feb 18, 2000) in view of Viguera et al. (Protein science 1999. 8:1733-1742) and Prieto et al. (J. Mol. Biol. 1997. 274: 276-288) is withdrawn in response to Applicant's amendment.

Claim Rejections/Objections Maintained

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. The rejection of claims 1-9, 11-24 under 35 U.S.C. 112, first paragraph, because the specification does not enable the invention commensurate in scope with the claims is maintained for reasons of record in the previous office action. The rejection is also applied to new claims 27-29 since new claims 27-29 are also within the scope of the original claims.

8. Applicant argues that the amended claims are enabled because they do not specify a particular use. Applicant's arguments have been fully considered but they are not persuasive. The amended claims are directed to a peptide comprising SEQ ID NO:8 to antagonize toxic or vitality-damage noxae of neurodegenerative diseases as recited in claims 1, 27 and 29, therapy of diseases with increased free radicals as recited in claim 11, therapy of diseases associated with acute hypoxia or ischemia as recited in claim 12, therapy of Recklinghausen-Appelbaum diseases as recited in claim 13, therapy of neurodegenerative diseases as recited in claim 14. The rest of claims depend from the claims as mentioned above.

9. Based on the specification, Applicant is enabled for protecting neurons in vitro from conditions of serum withdrawal, addition of ionomycin, chronic stress of iron chloride/hydrogen peroxide and apoptosis caused by amyloid-beta aggregation.

However, the claims are not limited to the in vitro condition as set forth above because they read on both in vitro and in vivo and the claims also recited the use of therapy of different diseases. Applicant fails to provide sufficient guidance or any working example as to enable one of skill in the art to treat any pathological conditions as recited in the claims 1, 27, 29 and 11-14. Applicant fails to demonstrate the results derived from in vitro can be reproduced in treating diseases in vivo as recited in claims 11-14 since the in vivo system is more complex than the well-controlled in vitro condition. The in vivo condition involves the efficacy, penetration, targeting and stability of the peptide in a biological system. In addition, different diseases have different causes and potential molecular mechanisms. Applicant fails to provide sufficient guidance or any working example to teach how to use the claimed invention in treating the diseases as recited in claims 11-14 and thus it is unpredictable whether the claimed peptide is effective in treating the diseases recited in the claims. Accordingly, it would appear that Applicant provides a finding, and then presents an invitation to experiment to determine whether these peptides are useful for treating the diseases as claimed and determine how to use the peptides to treat patients with different diseases and determine how to use the peptides to treat the patients with the guidance of the route, duration and quantity of administration of a peptide to a subject. Thus, the instant specification, as filed, provides insufficient guidance or no working example as to enable one skilled in the art to practice the claimed invention as recited in claims 11-24, thereby requiring undue experimentation to discover how to use the claimed invention. Thus, the rejection of claims 1-9, 11-24 and 27-29 under 35 U.S.C. 112, first paragraph, because the

specification does not enable the invention commensurate in scope with the claims is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. The rejection of claim 20 under 35 U.S.C. 112, second paragraph, for being indefinite because of the recitation "implants" is maintained for reasons of record in the previous office action. Applicant argues that administration via an active ingredient containing implants is clear in the art. Applicant's arguments have been fully considered but they are not persuasive. There are two separate requirements set forth in the 35 U.S.C. 112 2nd paragraph: (A) the claims must set forth the subject matter that applicants regard as their invention; and (B) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant. Claims are indefinite because Applicant fails to describes/specify what is encompasses within the implants. Although the general meaning of implants is known in the art, the disclosure fails to set forth the metes and bounds of what is encompassed within the definition of such implants. It is unclear what implants applicant is intending to encompass and thus the claim is indefinite.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims1-9, 11-24 and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO200160794 (published Aug 23, 2001, PCT/US01/05569, filed Feb 20, 2001, priority date Feb 18, 2000 as cited in the previous office action) in view of Volkmann et al. (EXS, 1998, 85: 87-105 as cited in the previous office action), Viguera et al. (Protein science 1999. 8:1733-1742 as cited in the previous office action) and Prieto et al. (J. Mol. Biol. 1997. 274: 276-288 as cited in the previous office action) as applied to original claims 1-9, 11-24 for reasons of record the previous office action, and further in view of Jensen et al. (Biochem. J. 1995. 310: 91-94).

12. WO200160794 ('794) teaches a beta-synuclein peptide (1-15 amino acids) for suppression of alpha-synuclein aggregation, which has 100% identity to the instant SEQ

ID NO:1 and SEQ ID NO:8. '794 also teaches different modifications on the peptide at the C-terminus and acetylation at the N-terminus and amidation at the C-terminus of the peptide to preserve the stability of the peptide (see p. 37, lines 14-20). '794 further teaches several ways of formulation for different administration routes for example intravenous or others including encapsulation in liposomes, microparticles, microcapsules for different administration routes as recited in claims 15-24 (see p. 10, line27 to p.12, line 18; p13, lines 13-20) as described in the previous office action. But '794 fails to teach shortening the beta-synuclein peptide to consist of an amino acid sequence less than 15 amino acids as recited in claims 1 and 29.

13. Jensen et al. teaches that KTKEGV is responsible for the formation of insoluble amyloid deposits and is involved in modification in different members of the synuclein family. Jensen et al. teaches transglutaminase catalyzes the formation of non-Abeta component of AD amyloid polymers and polymers of β-amyloid peptides (see p. 91, abstract). Jensen et al. teaches that transglutaminase-reactive amino acid residues are Gln^{79} and Lys^{80} and Lys^{80} is in a consensus motif of KTKEGV, which is conserved in synuclein gene family (see p.91, abstract). The teaching of the essential motif of beta synuclein to aggregate with β-amyloid peptides (i.e.KTKEGV) provides a motivation and expectation of success in shortening the amino acid sequence of the 15-aa beta-synuclein peptide because KTKEGV is essential for aggregation of beta synuclein with β-amyloid peptides and is also essential for transglutaminase activity to catalyze the formation of amyloid peptide deposits.

14. The teaching of the 15-amino acid beta-synuclein peptide in blocking aggregation of synuclein with b-amyloid peptide by WO200160794 provides a motivation and expectation of success in protecting neuronal death caused by amyloid aggregation with synuclein. The teachings of Jensen et al. indicate that KEGV of synuclein is essential for the activity of transglutaminase and for aggregation of synuclein with β-amyloid peptides. The teachings of acetylation at the N-terminus and amidation at the C-terminus provide a motivation and expectation of success in different modification as recited in claims 7-9. In addition, the natural occurring amino acids in proteins/peptides are L-amino acids and few are D-amino acids after post-translational modification as evidenced by Volkmann et al. (EXS, 1998, 85: 87-105 as cited in the previous office action).

15. Thus, it would have been obvious to one of skill in the art to shorten the amino acid sequence since a 15-amino acid beta synuclein peptide (SEQ ID NO:1) is able to block the formation of Aβ aggregation and KEGV is essential and required for the activity transglutaminase to break down Aβ aggregation. One of skill in the art would have been motivated to shorten the peptide that contain a minimum motif required for blocking aggregation of Aβ and further to protect neuronal damage caused by Aβ aggregation with synuclein because KTKEGV is conserved and required for the activity of transglutaminase to catalyze amyloid peptide aggregation with beta synuclein. The intended use for antagonizing the toxic and vitality-damaging noxae of neurodegenerative diseases as recited in claims 1, 11-14, 27 and 29 are not given patentable weight because the peptide and the peptide encompassed in the

composition are able to perform the same activity as in the 15-amino acid beta synuclein. The peptides encompassing the minimum residues and with a shorter length as disclosed the instant application are obvious variants of the 15-aa beta synuclein peptide as disclosed in '794.

16. In addition, '794 fails to teach D-amino acids as recited in claim 3 and fails to teach proline substitution at the N- and C-terminus as recited in claims 4-6.

17. Volkman et al. teach D-amino acids provide several advantages for a peptide/protein including increased potency and protease stability and a novel tertiary structure that could not be accessed from L-amino acids (see p.87, abstract). The teachings of Volkman et al. provide a motivation and a reasonable expectation of success to generate a peptide with D-amino acids as recited in claim 3.

18. Viguera et al. teach modification of an amino acid in a peptide with proline at N-terminus of the peptide can enhance the stability of the peptide (see p. 1733, abstract; p.1734, 1st col. 3rd paragraph) as recited in claims 4-6. Prieto et al. teach modification of an amino acid in a peptide with proline at C-terminus of the peptide can enhance the stability of the peptide (see p. 276, abstract) as recited in claims 4-6. The teachings of Viguera et al. and Prieto et al. provide a motivation and expectation of success in modifying the peptides with proline at N-terminus or C-terminus to increase the stability of the peptide.

19. It would have been obvious to one of ordinary skill in the art at the time of the instant invention was made to generate a β-synucleic peptide that blocks the Aβ

aggregation by using D-amino acids. The person of ordinary skill in the art would have been motivated to make that modification because D-amino acids can be used to increase the potency and protease stability. In addition, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the peptide with proline substitution at both N- and C-termini to enhance the stability of the peptide. Since proline substation at N-terminus or C-terminus can enhance the stability of the peptide, the person of ordinary skill in the art would have been motivated to make that modification to enhance the protease/thermal stability of the peptide and prevent the degradation of the peptide in a biological system because a biological system contains a lot of proteases to degrade the peptide. The person in the art would have expected success in enhancing the potency of the peptide in a biological system by enhancing the stability of the peptide to generate such peptide for the purpose of blocking Aβ aggregation or other pharmaceutical purposes.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang, Ph.D. whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday and every other Friday from 8:30 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CYW
March 22, 2007

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER